

Treatment of pharyngeal gonorrhoea due to β -lactamase-producing gonococci

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SUMMARY Between March 1978 and October 1980 seven patients with β -lactamase-producing gonococci in the pharynx were treated with spectinomycin or cefuroxime or both. One-day treatment with spectinomycin was effective in only one of six patients and with cefuroxime in only one of four patients. Prolonged treatment with cefuroxime was successful in all five cases so treated.

Introduction

During the last few years an increasing number of genital infections caused by β -lactamase-producing gonococci (PPNG) has been found in Sweden.¹ Most of these have been contracted abroad, usually in the Far East. So far there has only been a limited spread within Sweden and most of the indigenous cases have been direct contacts of a patient infected abroad.

Gonococcal infections of the pharynx are not uncommon among patients with genital gonorrhoea and are seen among both heterosexuals and homosexuals.² During 1980 gonococci were isolated from the pharynx in 110 out of the 795 (14%) patients treated for gonorrhoea in our clinic.

When the first patient with pharyngeal gonorrhoea caused by PPNG attended our clinic in 1978, there was some uncertainty about treatment, and various regimens were tried. This study reports the symptoms and treatment of patients with such infections.

Patients and methods

STUDY POPULATION

At the venereal disease clinic at Södersjukhuset, Stockholm, β -lactamase-producing *Neisseria gonorrhoeae* were isolated from 17 patients between March 1978 and October 1980. Cultures were generally taken from the urethra, cervix, rectum, and pharynx of women and from the urethra and pharynx of men. Cultures from the pharynx were obtained from all patients infected with PPNG strains; PPNG were isolated from this site in five men and three women. One man did not complete his treatment and was excluded from the study.

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All four men had contracted their infections in Thailand, one woman was infected in Portugal, and the remaining two were infected in Sweden by men who had recently been abroad in Thailand and Spain.

After treatment the patients were usually followed for a period of four weeks and cultures performed at least four times.

CULTURE TECHNIQUES

Specimens were taken with cotton swabs treated with charcoal. Each swab was immediately inoculated on to GC agar medium, consisting of Columbia blood agar base (Oxoid CM 331) supplemented with blood heated to approximately 80°C and with sterile GC supplement (Oxoid SR 56) containing vancomycin, colistin, trimethoprim, and nystatin, and on a medium of the same composition, to which sterile GC antibiotic supplement without antibiotics (Oxoid SR 62) had been added. The plates were immediately incubated at 37°C in a candle jar for a few hours before transport to the bacteriological laboratory in an adjoining building, where incubation was continued at 37°C in an atmosphere of 5% CO₂ for 48 hours. The plates were read by a plate microscope. Gonococci were identified by the oxidase test, microscopy, fermentation of dextrose but not maltose and levulose, and the coagglutination test (Phadebact, Pharmacia).

SENSITIVITY TESTING

Sensitivity tests were carried out by the agar diffusion method³ on GC agar medium using antibiotic discs (Biodisk, Stockholm). All isolates were tested for β -lactamase production with chromogenic cephalosporin (Biodisk, Stockholm, Sweden) and, for most strains, also by modified Escamilla⁴ and clover leaf⁵ techniques.

Results

SENSITIVITY TO ANTIBIOTICS

The sensitivity pattern of the *N gonorrhoeae* strains isolated from the seven patients with pharyngeal infection is summarised in table I. The sensitivity pattern was similar for most of the strains. All were found to produce β -lactamase by all three methods used. They were all sensitive to spectinomycin and cefuroxime.

TABLE I Antibiotic sensitivity (MIC) of seven β -lactamase-producing strains of *N gonorrhoeae* isolated from pharyngeal swabs

Antibiotic	MIC range (μ g/ml)
Benzylpenicillin	>8
Ampicillin	>16
Cephalosporin	4-8
Erythromycin	0.25-1
Clindamycin	0.5-4
Tetracycline	0.125-2
Chloramphenicol	1-16
Gentamicin	2-64
Fusidic acid	4-16
Spectinomycin	8-16
Cefuroxime	0.25-1

In one patient two different β -lactamase-producing strains were isolated. They differed significantly in their sensitivity to erythromycin, lincomycin, and rifampicin.

CLINICAL SYMPTOMS

The clinical symptoms reported by the seven patients are summarised in table II.

TABLE II Clinical symptoms in seven patients with β -lactamase-producing *N gonorrhoeae* in pharyngeal cultures

Symptoms	Men (4)	Women (3)	Total
Genital discharge	4	2	6
Fever	2	2	4
Sore throat	2	1	3
Arthralgia	0	1	1
Epididymitis	1	0	1
None	0	1	1

TREATMENT

The standard treatment for gonorrhoea given in our clinic consists of pivampicillin (1.4 g) with probenecid (1.0 g) at the first visit if the microscopy results are positive. At the second visit one week later the treatment is adjusted according to the results of the culture and sensitivity test carried out at the first visit. Six of the patients with PPNG in the pharynx were thus initially treated with pivampicillin.

Regimens (A) and (B)

During the first part of the study spectinomycin was usually given at the second visit, but later when cefuroxime became available this drug was introduced for the treatment of infections with PPNG. Owing to the therapeutic failures different doses have been given and the same patients have sometimes received several courses of treatment. The treatment schedules have been classified as 'one day' treatment (A) or 'more than one day' treatment (B). The results are summarised in table III.

TABLE III Results of different treatment regimens

Treatment	No of cures/total No of treatments for gonorrhoea of:	
	Pharynx	Urethra
Regimen (A)*		
Pivampicillin		
1.4 g or 2.45 g plus probenecid 1.0 g	0/5	0/4
Spectinomycin		
2.0 g	0/3	3/3
2.0 g \times 3 doses	1/2	1/1
4.0 g	0/1	
Total	1/6	4/4
Cefuroxime		
1.5 g	0/1	
0.75 g + probenecid 1.0 g	0/1	
1.0 g + probenecid 1.0 g	1/1	
1.5 g \times 2 doses	0/1	
Total	1/4	
Regimen (B)*		
Pivampicillin		
0.35 g \times 3 doses daily for 7 days	0/1	0/1
Spectinomycin		
2.0 g daily for 3 days	0/1	1/1
Cefuroxime		
1.5 g daily for 3 days	1/1	
1.5 g + probenecid 1.0 g daily for 3 days	1/1	1/1
0.75 g daily for 3 days	1/1	
0.75 g + probenecid 1.0 g daily for 3 days	1/1	
1.5 g \times 3 doses daily for 7 days	1/1	
Total	5/5	1/1

Regimen (A) = treatment for one day; regimen (B) = treatment for more than one day

Treatment (A) with spectinomycin cured the pharyngeal infection in only one of six cases; for cefuroxime the corresponding figure was one out of four. Treatment (A) with spectinomycin, however, cured the urethral infection in all of four patients.

Treatment (B) with spectinomycin was given to only one patient with pharyngeal infection, but without success. Treatment (B) with cefuroxime was successful in all of five cases.

TEST-OF-CURE CULTURES

The patients were considered to be cured when at least four culture results were negative during a

period of at least four weeks. In five inpatients throat swabs for culture were usually taken three times a day during treatment and for the following few days. Treatment with spectinomycin or cefuroxime gave negative culture results within a few hours of injection. In most cases of therapeutic failure the culture results became positive again within less than a week. In one case, however, gonococci were not isolated until the fourth culture taken three weeks after treatment (figure). In none of the cases were the positive culture results after treatment believed to be due to reinfection.

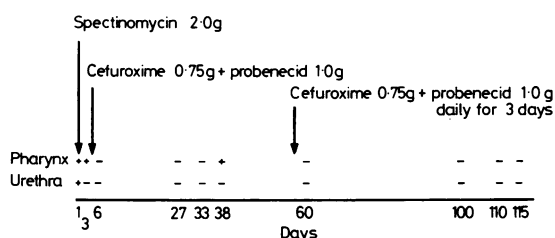


FIGURE Results of cultures and treatment given to one patient.

Discussion

Pharyngeal infections with penicillin-sensitive *N gonorrhoeae* are more difficult to treat than anogenital gonorrhoea. Bro-Jørgensen and Jensen⁶ reported that only 60% of their 93 patients were cured by a single dose of ampicillin, pivampicillin, or penicillin G with probenecid compared with almost 100% of patients with anogenital infections. This agrees with our own experience.

Wiesner *et al*⁷ reported that spectinomycin had a poor effect on pharyngeal gonorrhoea caused by non-PPNG strains. These results were not confirmed in the five patients with pharyngeal infection caused by PPNG strains in the US PPNG surveillance study.⁸ In the present study different spectinomycin regimens were, therefore, tried before cefuroxime became available. Our results indicate that although treatment with a single dose of spectinomycin may be sufficient to cure an urethral infection with PPNG, the pharyngeal infection is usually not cured. Our data do not allow any conclusions about the effectiveness of prolonged treatment with spectinomycin.

Jones *et al*⁹ reported that one-day treatment with 1 g or 2 g of cefoxitin was not sufficient to eradicate oropharyngeal carriage of *N gonorrhoeae*, although the urogenital infection was cured in all 25 cases studied.

Moberg and Wennberg¹⁰ reported successful treatment of 38 out of 39 female patients with urogenital gonorrhoea with 1 g of cefuroxime intramuscularly in combination with 1 g probenecid orally.

In the present study only one of four patients with pharyngeal gonorrhoea was cured by a single dose of cefuroxime. When the treatment with cefuroxime was extended for three days or more, however, all five patients were cured of pharyngeal gonorrhoea clinically and bacteriologically.

The importance of repeated cultures after treatment is clearly seen in our study. After treatment with both spectinomycin and cefuroxime culture results may initially be negative only to become positive later.

Although there is a tendency to regard gonococci in the pharynx as colonisation without clinical importance,¹¹ Wiesner *et al*⁷ found an increased incidence of pharyngeal infection among heterosexual men with disseminated gonococcal infection. In this context it is of interest that four of seven of our patients with pharyngeal infection caused by PPNG strains had fever, one had arthralgia, and one epididymitis, although PPNG strains are not considered to be more virulent than non-PPNG strains.⁸

The high incidence of pharyngeal infection in patients with PPNG (47% in our series) is of concern because of the coexistence of meningococci in patients with pharyngeal gonococcal infection reported by Noble *et al*.¹² Experimentally, genetic information is readily exchanged between different *Neisseria* species¹³ and the transfer of the β -lactamase plasmid to meningococci is a possibility. Even if the epidemiological significance of the presence of gonococci in the pharynx is not clear¹¹ it, therefore, seems reasonable to eliminate the PPNG strains as quickly as possible.

From our experience we propose the following management of patients with anogenital PPNG strains: (a) at least two cultures should be obtained from the pharynx before a pharyngeal infection is excluded; (b) patients with a pharyngeal PPNG infection should be treated with 1500 mg cefuroxime intramuscularly once daily for three days or 750 mg cefuroxime intramuscularly and 1 g probenecid orally once daily for three days; and (c) after treatment of pharyngeal infection four negative culture results should be obtained over a four-week period to confirm complete cure.

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